EXHIBIT B

Documents Produced in Core Discovery:

- Letter to FDA dated 03/02/2011 regarding Drug Master File (Type II), Subject: Valsartan USP (Process II), DMF # 024544 (APL-MDL 2875-0016073 to -0016074)
- Statement of Commitment re: DMF # 024544 (APL-MDL 2875-0016075)
- Administrative Page (APL-MDL 2875-0016076 to -0016077)
- US Agent Appointment Letter (APL-MDL 2875-0016078)
- Letter to FDA dated 03/02/2011 re: Debarment Certification (APL-MDL 2875-0016079)
- Valsartan USP (Process II) Declaration of Residual Solvents (03/02/2011) (APL-MDL 2875-0016068)
- Transmittal Letter re: DMF Type II, Valsartan USP (Process II) (APL-MDL 2875-0016069)
- Environmental Assessment (Valsartan USP Process II) (APL-MDL 2875-0016072)
- DMF Valsartan USP (Process II) Module 2 Quality Overall Summary (APL-MDL 2875-0016038 to -0016067)
- 3.2.R.2 Control Numbers (APL-MDL 2875-0016892 to -0016894)
- 3.2.R.1 Executed Batch Records (APL-MDL 2875-0016750 to -0016891)
- 3.2.R.3 Sample Availability and Identification (Reserve Samples) (APL-MDL 2875-0016748 to -0016749)
- 3.2.S.1.3 General Properties (APL-MDL 2875-0016110 to -0016112)
- 3.2.S.1.1 Nomenclature (APL-MDL 2875-0016113 to -0016114)
- 3.2.S.1.2 Structure (APL-MDL 2875-0016115 to -0016116)
- 3.2.S.2.4 Controls of Critical Steps and Intermediates (APL-MDL 2875-0016536 to -0016539)
- Certificates of Analysis (APL-MDL 2875-0016482 to APL-MDL 2875-0016486)
- Intermediate Specification of N-[(2'-Cyanobiphenyl-4-YL)Methyl]-(L)-Valine Methyl Ester – Toluene Solution (Valsartan Step-I) (APL-MDL 2875-0016504)

- Intermediate Specification of N-[(2'-Cyanobiphenyl-4-YL)Methyl]-(L)-Valine Methyl Ester – Toluene Solution (Valsartan Step-II) (APL-MDL 2875-0016512)
- In-Process Specification of N-[(2'-Cyanobiphenyl-4-YL)Methyl]-(L)-Valine Methyl Ester – Toluene Solution (Valsartan Step-I) (APL-MDL 2875-0016495)
- In-Process Specification of N-[(2'-Cyanobiphenyl-4-YL)Methyl]-(L)-Valine Methyl Ester (Valsartan Step-II) (APL-MDL 2875-0016499)
- In-Process Specification of N-(1-Oxopentyl)-N-[[2'-(2-Tributyltin Tetrazol-5-YL)-(1,1'-Biphenyl)-4-YL]Methyl]-(L)-Valine Methyl Ester (Valsartan Step-III) (APL-MDL 2875-0016503)
- In-Process Specification of Valsartan USP (Process II) [Step IV] (APL-MDL 2875-0016510)
- In-Process Test Procedure: Valsartan Step-I (APL-MDL 2875-0016487 to -0016488)
- In-Process Test Procedure: Valsartan Step-II (APL-MDL 2875-0016497 to -0016498)
- In-Process Test Procedure: Valsartan Step-III (APL-MDL 2875-0016566 to -0016567)
- In-Process Test Procedure: Valsartan USP (Process II) [Step-IV] (APL-MDL 2875-0016542 to -0016545)
- 3.2.S.2 Manufacturer(s) (APL-MDL 2875-0016505 to -0016507)
- 3.2.S.2.6 Manufacturing Process Development (APL-MDL 2875-0016491 to -0016492)
- 3.2.S.2.5 Process Validation and/or Evaluation (APL-MDL 2875-0016550 to -0016554)
- 3.2.S.2.3 Control of Materials (APL-MDL 2875-0016519 to -0016530)
- 3.2.S.2.2 Description of Manufacturing Process and Process Controls with Batch Production and Control Records (APL-MDL 2875-0016576 to -0016745)
- Specification No. SRM31201 2,6-Lutidine (APL-MDL 2875-0016464)
- Specification No. SRM 31101 2-(4'Bromotheylphenyl) Benzonitrile (APL-MDL 2875-0016470)
- Specification No. SRM00201 Carbon Enoanticromos (APL-MDL 2875-0016502)
- Specification No. SRM01701 Ethyl Acetate (APL-MDL 2875-0016518)

- Specification No. SRM00801 Hydrochloric Acid (CP grade) (APL-MDL 2875-0016463)
- Specification No. SRM00901 Hyflo Supercel (APL-MDL 2875-0016476)
- Specification No. SRM15801 L-Valine Methyl Ester Hydrochloride (APL-MDL 2875-0016571)
- Specification No. SRM02401 Sodium Hydroxide (Caustic Soda Flakes) (APL-MDL 2875-0016496)
- Specification No. SRM16601 Potassium Carbonate (Anhydrous) (APL-MDL 2875-0016557)
- Specification No. SWM00304 Purified Water (APL-MDL 2875-0016483)
- Specification No. SRS12301 Recovered Ethyl Acetate [Valsartan Step-I (Process II)] (APL-MDL 2875-0016480)
- Specification No. SRS11901 Recovered Ethyl Acetate [Valsartan USP (Process II)] (pH adjusted at 2-2.5) (APL-MDL 2875-0016493)
- Specification No. SRS12401 Recovered Toluene [Valsartan Step-III (Process II)] (APL-MDL 2875-0016472)
- Specification No. SRM05401 Refined Sodium Chloride (APL-MDL 2875-0016559)
- Specification No. SRM05001 Sodium Azide (APL-MDL 2875-0016535)
- Specification No. SRM06701 Sodium Carbonate (Anhydrous) (APL-MDL 2875-0016568)
- Specification No. SRM26601 Sodium Nitrite (APL-MDL 2875-0016508)
- Specification No. SRM03601 Toluene (APL-MDL 2875-0016501)
- Specification No. SRM23901 Tri n-Butyl Tin Chloride (APL-MDL 2875-0016549)
- Specification No. SRM15901 Valeryl Chloride (APL-MDL 2875-0016467)
- Standard Test Procedure: 2,6-Lutidine (APL-MDL 2875-0016574)
- Test Procedure: 2-(4’Bromotheylphenyl) Benzonitrile (APL-MDL 2875-0016473 to -0016475)
- Standard Test Procedure: Carbon Enoanticromos (APL-MDL 2875-0016531 to -0016533)

- Standard Test Procedure: Ethyl Acetate (APL-MDL 2875-0016564 to -0016565)
- Test Procedure: Hydrochloric Acid (CP Grade) (APL-MDL 2875-0016484 to -0016485)
- Standard Test Procedure: Hyflo Supercel (APL-MDL 2875-0016465)
- Testing Procedure: L-Valine Methyl Ester Hydrochloride (APL-MDL 2875-00165560 to -0016561)
- Test Procedure: Sodium Hydroxide (Caustic Soda Flakes) (APL-MDL 2875-0016572 to -0016573)
- Standard Test Procedure: Potassium Carbonate (Anhydrous) (APL-MDL 2875-0016477)
- Standard Test Procedure: Purified Water (APL-MDL 2875-0016746)
- Test Procedure: Recovered Ethyl Acetate [Valsartan Step-I (Process II)] (APL-MDL 2875-0016481)
- Test Procedure: Recovered Ethyl Acetate [Valsartan USP (Process II)] (pH adjusted at 2-2.5) (APL-MDL 2875-0016558)
- Test Procedure: Recovered Toluene [Valsartan Step-III (Process II)] (APL-MDL 2875-0016489)
- Standard Test Procedure: Refined Sodium Chloride (APL-MDL 2875-0016515)
- Standard Test Procedure: Sodium Azide (APL-MDL 2875-0016569)
- Standard Test Procedure: Sodium Carbonate (Anhydrous) (APL-MDL 2875-0016541)
- Standard Test Procedure: Sodium Nitrite (APL-MDL 2875-0016478)
- Standard Test Procedure: Toluene (APL-MDL 2875-0016546)
- Standard Test Procedure: Tri n-Butyl Tin Chloride (APL-MDL 2875-0016575)
- Standard Test Procedure: Valeryl Chloride (APL-MDL 2875-0016570)
- 3.2.S.3.1 Elucidation of Structure and Other Characteristics (APL-MDL 2875-0016140 to -0016155)
- 3.2.S.3.2 Impurities (APL-MDL 2875-0016127 to -0016139)

- 3.2.S.4.1 Specification (APL-MDL 2875-0016459 to -0016462)
- 3.2.S.4.2 Analytical Procedures (APL-MDL 2875-0016176 to -0016187)
- Validation of Stability Indicating HPLC Method for the Assay of Valsartan Drug Substance (APL-MDL 2875-0016336 to -0016392)
- Validation of HPLC Method for the Determination of Limit of Valsartan Enantiomer (USP Related Compound A) in Valsartan Drug Substance (APL-MDL 2875-0016292 to -0016335)
- Validation of Stability Indicating HPLC Method for the Determination of Related Substances in Valsartan Drug Substance (APL-MDL 2875-0016213 to -0016289)
- Validation of Head Space-GC Method for the Determination of Residual Solvents in Valsartan Drug Substance (APL-MDL 2875-0016393 to -0016458)
- 3.2.S.4.3 Validation Analytical Procedure (APL-MDL 2875-0016290 to -0016291)
- 3.2.S.4.4 Batch Analyses (APL-MDL 2875-0016205 to -0016212)
- 3.2.S.4.5 Justification of Specifications (APL-MDL 2875-0016188 to -0016204)
- 3.2.S.5 Reference Standards or Materials (APL-MDL 2875-0016080 to -0016109)
- 3.2.S.6 Container Closure System (APL-MDL 2875-0016117 to -0016126)
- 3.2.S.7.2 Post Approval Stability Protocol and Commitments (APL-MDL 2875-0016174 to -0016175)
- 3.2.S.7.3 Stability Data (APL-MDL 2875-0016156 to -0016169)
- 3.2.S.7.1 Stability Summary and Conclusions (APL-MDL 2875-0016170 to -0016173)
- Amendment # 1 to DMF # 02544
    - Cover Letter re: DMF # 024544 DMF Amendment # 1 (July 19, 2011) (APL-MDL 2875-0011063 to -0011064)
    - Letter of Authorization – M/s. Forest Laboratories, Inc. (April 1, 2011) (APL-MDL 2875-0011056)
    - Letter of Authorization – M/s Aurobindo Pharma Limited (April 25, 2011) (APL-MDL 2875-0011059 to -0011060)

- Letter of Authorization – M/s. Aurobindo Pharma Limited (July 15, 2011) (APL-MDL 2875-0011057 to -0011058)
- 3.2.S.4.1 Specification (APL-MDL 2875-0011121 to -0011124)
- 3.2.S.4.2 Analytical Procedures (APL-MDL 2875-0011083 to -0011095)
- 3.2.S.4.4 Batch Analyses with Certificates of Analysis (APL-MDL 2875-0011113 to -0011120)
- 3.2.S.4.5 Justification of Specifications (APL-MDL 2875-0011096 to -0011112)
- 3.2.S.7.1 Stability Summary and Conclusions (APL-MDL 2875-0011079 to -0011082)
- 3.2.S.7.3 Stability Data (APL-MDL 2875-0011065 to -0011078)

- Amendment # 2
  - Cover Letter re: Amendment – 2 to Type II Drug Master File, Valsartan USP (Process II), DMF # 024544 (May 8, 2012) (APL-MDL 2875-0016942 to -0016958)
  - Letter of Authorization – M/s. Natco Pharma Limited (April 5, 2012) (APL-MDL 2875-0016940)
  - Blank BPCRS of Step I II III and IV (APL-MDL 2875-0017003 to -0017168)
  - Certificates of Analysis
    - L-Valine Methyl Ester Hydrochloride (APL-MDL 2875-0017185)
    - Valeryl Chloride (APL-MDL 2875-0017186)
    - Recovered 2,6-Lutidine (from Valsartan Stage-IB) (APL-MDL 2875-0017172)
    - Recovered Ethyl Acetate [Crystallization of Valsartan (Process II)] (APL-MDL 2875-0017182)
    - Recovered Toluene [Valsartan (Process II)] (APL-MDL 2875-0017177)
    - Recovered Toluene [Valsartan Stage-IA (Process II)] (APL-MDL 2875-0017170)
    - Recovered Toluene [Valsartan Stage-IB (Process II)] (APL-MDL 2875-0017183)

- Tri-n-Butyl Tin Chloride (Recovery from Valsartan Stage-I) (APL-MDL 2875-0017176)
- Recovered 2,6-Lutidine [Valsartan Step-II (Process II)]

- Standard Test Procedure: Recovered 2,6-Lutidine [Valsartan Step-II (Process II)] (APL-MDL 2875-0017173)
- Specification No. SIN16401 Recovered 2,6-Lutidine [Valsartan Step-II (Process II)] (APL-MDL 2875-0017174)
- Specification No. SRM15802 L-Valine Methyl Ester Hydrochloride (APL-MDL 2875-0017192)
- Specification No. SRS12001 Recovered Ethyl Acetate (Crystallization of Valsartan USP (Process II) (APL-MDL 2875-0017180)
- Specification No. SRS11701 Recovered Toluene [Valsartan USP (Process II)] (APL-MDL 2875-0017187)
- Specification No. SRS11501 Recovered Toluene [Valsartan Step-I (Process II)] (APL-MDL 2875-0017171)
- Specification No. SRS19301 Recovered Toluene [Valsartan Step-II (Process II)] (APL-MDL 2875-0016999)
- Specification No. SIN16001 Recovered Tri-N-Butyl Tin Chloride [Valsartan USP (Process II)] (APL-MDL 2875-0017184)
- Specification No. SRM15901 Valeryl Chloride (APL-MDL 2875-0017169)
- Testing Procedure: L-Valine Methyl Ester Hydrochloride (APL-MDL 2875-0017188 to -0017190)
- Test Procedure: Recovered Ethyl Acetate [Crystallization of Valsartan USP (Process II)] (APL-MDL 2875-0017178)
- Test Procedure: Recovered Toluene [Valsartan USP (Process II)] (APL-MDL 2875-0017181)
- Test Procedure: Recovered Toluene [Valsartan Step-I (Process II)] (APL-MDL 2875-0017001 to -0017002)
- Test Procedure: Recovered Toluene [Valsartan Step-II (Process II)] (APL-MDL 2875-001700)

- Test Procedure: Recovered Toluene [Valsartan Step-III (Process II)] (APL-MDL 2875-0017175)
- Test Procedure: Recovered Tri-N-Butyl Tin Chloride [Valsartan USP (Process II)] (APL-MDL 2875-0017179)
- Standard Test Procedure: Valeryl Chloride (APL-MDL 2875-0017191)
- 3.2.S.4.2 Analytical Procedures (APL-MDL 2875-0016981 to -0016994)
- Batch Analyses Valsartan USP (Process II) (APL-MDL 2875-0016995 to -0016998)
- 3.2.S.7.3 Stability Data (APL-MDL 2875-0016959 to -0016976)
- 3.2.S.7.1 Stability Summary and Conclusions (APL-MDL 2875-0016977 to -0016980)

- Amendment # 3
  - Cover Letter re: Amended – 3 to Type II Drug Master File, Valsartan USP (Process II), DMF # 024544 (April 19, 2013) (APL-MDL 2875-0016911 to -0016912)
  - Letter of Authorization – M/s. Forest Laboratories, Inc. (March 22, 2013) (APL-MDL 2875-0016909)
  - Certificate of Analysis – Purified Water (APL-MDL 2875-0016936)
  - Specification No. SWM00304 Purified Water (APL-MDL 2875-0016935)
  - 3.2.S.7.3 Stability Data (APL-MDL 2875-0016913 to -0016930)
  - 3.2.S.7.1 Stability Summary and Conclusions (APL-MDL 2875-0016931 to -0016934)

- Stand Alone Amendment
  - Generic Drug User Fee Cover Sheet (Form FDA 3794) (APL-MDL 2875-0010108 to -0010111)
  - Cover Letter re: Amendment to Type II DMF # 024544 (August 30, 2013) (APL-MDL 2875-0010107)
  - Letter of Authorization – M/s. Aurobindo Pharma Limited (August 29, 2013) (APL-MDL 2875-0010103 to -0010104)

- Amendment # 4
    - Cover Letter re: Amendment – 4 to Type II Drug Master File, Valsartan USP (Process II), DMF # 024544 (APL-MDL 2875-0010124 to -0010161)
    - Letter of Authorization – M/s. Aurobindo Pharma Limited (November 19, 2013) (APL-MDL 2875-0010121 to -0010122)
    - Batch Production and Control Records (APL-MDL 2875-0010710 to -0011042)
    - Certificate of Analysis (APL-MDL 2875-0011049 to -0011051)
    - Recovered Ethyl Acetate [Valsartan (Process II): pH adjusted at 2-2.5)] Specification No. SRS11901, Test Procedure, Certificate of Analysis (APL-MDL 2875-0011043 to -0011045)
    - Recovered Ethyl Acetate [Valsartan Stage-IA (Process II)] Specification No. SRS12301, Test Procedure, Certificate of Analysis (APL-MDL 2875-0011046 to -0011048)
    - 3.2.S.3.2 Impurities (APL-MDL 2875-0010162 to -0010178)
    - 3.2.S.4.3 Validation of Analytical Procedures (APL-MDL 2875-0010253 to -0010709)
    - 3.2.S.4.4 Batch Analyses with Certificates of Analysis (APL-MDL 2875-0010221 to -0010252)
    - 3.2.S.7.3 Stability Data (APL-MDL 2875-0010179 to -0010220)
- Amendment # 5
    - Cover Letter re: Amendment-5 to Type II DMF # 024544 (May 4, 2016) (APL-MDL 2875-0018342 to -0018364)
    - Valsartan USP (Process II, o-Xylene Route) Declaration of Residual Solvents (May 4, 2016) (APL-MDL 2875-0018340)
    - 3.2.R.1 Executed Batch Records (APL-MDL 2875-0019509 to -0019740)
    - 3.2.S.2.4 Controls of Critical Steps and Intermediates (APL-MDL 2875-0019483 to -0019508)
    - 3.2.S.2.3 Control of Materials (APL-MDL 2875-0019221 to -0019232)

- L-Valine Specification No. SRM35501, Standard Testing Procedure, Certificate of Analysis (APL-MDL 2875-0019213 to -0019217)
- Description of Manufacturing Process and Controls o-Xylene Route (APL-MDL 2875-0019233 to -0019478)
- Methylene Chloride Specification No. SRM05201, Testing Procedure, Certificate of Analysis (APL-MDL 2875-0019209 to -0019212)
- Methanol Specification No. SRM01101, Testing Procedure, Certificate of Analysis (APL-MDL 2875-0019479 to -0019482)
- o-Xylene Specification No. SMR02601, Testing Procedure, Certificate of Analysis (APL-MDL 2875-0019218 to -0019220)
- 3.2.S.2.5 Process Validation and/or Evaluation (APL-MDL 2875-0019195 to -0019204)
- Thionyl Chloride Specification No. SRM02001, Standard Test Procedure, Certificate of Analysis (APL-MDL 2875-0019205 to -0019208)
- Elucidation of Structure of o-Xylene Route (APL-MDL 2875-0018397 to -0018413)
- 3.2.S.3.2 Impurities (APL-MDL 2875-0018376 to -0018396)
- Specification o-Xylene Route (APL-MDL 2875-0019191 to -0019194)
- Analytical Procedure o-Xylene Route (APL-MDL 2875-0018476 to -0018486)
- Validation of Analytical Procedures (APL-MDL 2875-0018545 to -0019190)
- 3.2.S.4.4 Batch Analyses (APL-MDL 2875-0018506 to -0018544)
- 3.2.S.4.5 Justification Specifications (APL-MDL 2875-0018487 to -0018505)
- 3.2.S.6 Container Closure System (APL-MDL 2875-0018365 to -0018375)
- 3.2.S.7.3 Stability Data (APL-MDL 2875-0018414 to -0018470)
- 3.2.S.7.1 Stability Summary and Conclusions (APL-MDL 2875-0018471 to -0018475)

- Amendment # 6

- Cover Letter re: Administrative amendment for change in address of DMF holder of Type-II Drug Master File, Valsartan USP (Process II), DMF # 024544 (May 11, 2016) (Change in Address of DMF Holder) (APL-MDL 2875-0010115 to -0010116)

- Amendment # 7
  - Cover Letter re: Amendment-7 to Type II DMF # 024544 (February 2, 2017) (APL-MDL 2875-0017311 to -0017332)
  - In-Process Test Procedure: Valsartan USP (Process II) [Step-IV] (APL-MDL 2875-0017457 to -0017460)
  - 3.2.S.2.2 Description of Manufacturing Process and Process Controls (APL-MDL 2875-0017461 to -0018335)
  - Recovered Ethyl Acetate (Valsartan Process II); (pH Adjusted at 2-2.5) Specification No. SRS11901, Test Procedure, Certificate of Analysis (APL-MDL 2875-0017449 to -0017451)
  - Standard Test Procedure: 2,6-Lutidine (APL-MDL 2875-0017452)
  - Standard Test Procedure: Recovered 2,6-Lutidine [Valsartan Step-II (Process II)] (APL-MDL 2875-0017448)
  - Recovered Toluene (From Tri-N-Butyltin Chloride Mixture of Valsartan API) Specification No. SRS37801, Test Procedure, Certificate of Analysis (APL-MDL 2875-0017453 to -0017456)
  - 3.2.S.4.4 Batch Analyses (APL-MDL 2875-0017403 to -0017447)
  - 3.2.S.7.3 Stability Data (APL-MDL 2875-0017333 to -0017397)
  - 3.2.S.7.1 Stability Summary and Conclusions (APL-MDL 2875-0017398 to -0017402)

- Amendment # 8
  - Cover Letter re: Administrative amendment for change in address of US Agent of Type-II Drug Master File, Valsartan USP (Process-II), DMF # 024544 (April 11, 2018) (APL-MDL 2875-0010096 to -0010097)
  - Administrative Page (APL-MDL 2875-0010098 to -0010099)
  - US Agent Appointment Letter (APL-MDL 2875-0010100)

- Amendment # 9
    - Cover Letter re: Valsartan USP (Process II), DMF # 024544 – DMF Information Request (August 7, 2018) (APL-MDL 2875-0020309 to -0020770)
- Amendment # 10
    - Cover Letter re: Amendment-10 to Type Drug Master File Valsartan USP (Process II) (November 14, 2018) (APL-MDL 2875-0020774 to -0020796)
    - 3.2.S.2.4 Controls of Critical Steps and Intermediates (APL-MDL 2875-0022122 to -0022146)
    - 3.2.S.2.3 Control of Materials (APL-MDL 2875-0021956 to -0022099)
    - Manufacturing Process and Controls o-Xylene (APL-MDL 2875-0021685 to -0021955)
    - Manufacturing Process and Controls Toluene (APL-MDL 2875-0022147 to -0023230)
    - Process Validation Toluene (APL-MDL 2875-0022100 to 0022121)
    - 3.2.S.3.2 Impurities (APL-MDL 2875-0020797 to -0020818)
    - Specification o-Xylene (APL-MDL 2875-0021677 to -0021680)
    - Specification Toluene (APL-MDL 2875-0021681 to 0021684)
    - Validation of Analytical Procedures (APL-MDL 2875-0020980 to -0021676)
    - Batch Analyses (APL-MDL 2875-0020906 to -0020979)
    - Justification Specifications (APL-MDL 2875-0020900 to -0020905)
    - 3.2.S.7.3 Stability Data (APL-MDL 2875-0020819 to -0020894)
    - 3.2.S.7.1 Stability Summary and Conclusions (APL-MDL 2875-0020895 to -0020899)
- Amendment # 11
    - Cover Letter re: Amendment-11 to Type II Drug Master File Valsartan USP (Process II) (December 19, 2018) (APL-MDL 2875-0017200 to -0017307)
- Amendment # 12

- Cover Letter re: Amendment-12 to Type II Drug Master File Valsartan USP (Process II) (April 15, 2019) (APL-MDL 2875-0011177 to -0011496)
- Letter of Authorization – M/s. Aurobindo Pharma Limited (March 1, 2019) (APL-MDL 2875-0011174 to -0011175)
- 3.2.R.2 Control Numbers (APL-MDL 2875-0013311 to -0013314)
- 3.2.R.1 Executed Batch Records (APL-MDL 2875-0013315 to -0013546)
- 3.2.S.2.4 Controls of Critical Steps and Intermediates (APL-MDL 2875-0012863 to -0012893)
- 3.2.S.2.3 Control of Materials (APL-MDL 2875-0012900 to -0013028)
- 3.2.S.2.1 Manufacturer(s) (APL-MDL 2875-0012894 to -0012899)
- 3.2.S.2.2 Description of Manufacturing Process and Process Controls with Batch Production and Control Records (APL-MDL 2875-0013029 to -0013310)
- 3.2.S.3.2 Impurities (APL-MDL 2875-0012016 to -0012035)
- 3.2.S.4.1 Specification Valsartan USP (Process II, o-Xylene Route) (APL-MDL 2875-0012859 to -0012862)
- 3.2.S.4.2 Analytical Procedures (APL-MDL 2875-0012056 to -0012084)
- 3.2.S.4.3 Validation of Analytical Procedures (APL-MDL 2875-0012123 to -0012858)
- 3.2.S.4.4 Batch Analysis (APL-MDL 2875-0012104 to -0012122)
- 3.2.S.4.5 Justification of Specifications (APL-MDL 2875-0012085 to -0012103)
- 3.2.S.5 Reference Standards or Materials with Certificates of Analysis (APL-MDL 2875-0011959 to -0011989)
- 3.2.S.6 Container Closure System (APL-MDL 2875-0011990 to -0012015)
- 3.2.S.7.3 Stability Data (APL-MDL 2875-0012036 to -0012051)
- 3.2.S.7.1 Stability Summary and Conclusions (APL-MDL 2875-0012052 to -0012055)

- Amendment # 13

- Cover Letter re: Valsartan USP (Process II), DMF # 024544 – General Advice (April 25, 2019) (APL-MDL 2875-0011129 to -0011171)

- Amendment # 14
  - Cover Letter re: Valsartan USP (Process II), DMF # 024544 – DMF Information Request (APL-MDL 2875-0019747 to -0020107)
  - 3.2.S.2.3 Control of Materials (APL-MDL 2875-0020132 to -0020304)
  - 3.2.S.3.2 Impurities (APL-MDL 2875-0020108 to -0020127)
  - 3.2.S.7.1 Stability Summary and Conclusions (APL-MDL 2875-0020128 to -0020131)

- Amendment # 15
  - Cover Letter re: Amendment-15 to Type II Drug Master File Valsartan USP (Process II) (October 1, 2019) (APL-MDL 2875-0013553 to -0013596)
  - 3.2.S.2.4 Controls of Critical Steps and Intermediates (APL-MDL 2875-0015421 to -0015453)
  - 3.2.S.2.3 Control of Materials (APL-MDL 2875-0015479 to -0015661)
  - 3.2.S.2.1 Manufacturer(s) (APL-MDL 2875-0015473 to -0015478)
  - 3.2.S.2.2 Description of Manufacturing Process and Process Controls (APL-MDL 2875-0015662 to -0015973)
  - 3.2.S.2.5 Process Validation and/or Evaluation (APL-MDL 2875-0015454 to -0015472)
  - 3.2.S.3.2 Impurities (APL-MDL 2875-0013597 to -0013616)
  - 3.2.S.4.1 Specification Valsartan USP (Process II, o-Xylene Route) (APL-MDL 2875-0015416 to -0015420)
  - 3.2.S.4.2 Analytical Procedures (APL-MDL 2875-0013639 to -0013687)
  - 3.2.S.4.3 Validation of Analytical Procedures (APL-MDL 2875-0013730 to -0015415)
  - 3.2.S.4.4 Batch Analyses (APL-MDL 2875-0013708 to -0013729)

  - 3.2.S.4.5 Justification of Specifications (APL-MDL 2875-0013688 to -0013707)
  - 3.2.S.7.1 Stability Summary and Conclusions (APL-MDL 2875-0013635 to -0013638)
  - 3.2.S.7.3 Stability Data (APL-MDL 2875-0013617 to -0013634)

- Amendment # 16
  - Cover Letter re: Amendment-16 to Type II Drug Master File Valsartan USP (Process II) (December 18, 2019) (APL-MDL 2875-0009969 to -0009972)
  - 3.2.S.3.2 Impurities (APL-MDL 2875-0009973 to -0010013)
  - 3.2.S.4.2 Analytical Procedures (APL-MDL 2875-0010043 to -0010088)
  - 3.2.S.7.1 Stability Summary and Conclusions (APL-MDL 2875-0010039 to -0010042)
  - 3.2.S.7.3 Stability Data (APL-MDL 2875-0010014 to -0010038)

- Summary of the Amendments Submitted to USFDA for Valsartan USP (Process II) (DMF # 024544) Related to Nitrosamine Impurities (APL-MDL 2875-0010119 to -0010120)
- Action Items: FDA Regulatory Meeting, July 24, 2019 (APL-MDL 2875-0023244 to -0023248)
- List of Documents provided to USFDA May 28, 2020 (APL-MDL 2875-0023249)
- Cover Letter dated October 4, 2013, and EIR for July 22-25, 2013, Inspection of APL Research Center-II (APL-MDL 2875-0028941 to -0028952)
- Cover Letter dated May 2, 2016, and EIR for December 2-4, 2015, Inspection of APL Research Center-II (APL-MDL 2875-0028953 to -0028961)
- EIR for January 7-10, 2020, Inspection of APL Research Center-II (APL-MDL 2875-0028924 to -0028939)
- APL Research Center-II USFDA Audit Details (APL-MDL 2875-0028940)
- Response to Observations Made in Form FDA 483 during June 4-8, 2012 Inspection of APL Unit XI
  - Cover Letter (June 27, 2012) (APL-MDL 2875-0009821 to -0009827)

  - List of Raw Material Vendors & Revised Manufacturer Qualification Questionnaire (APL-MDL 2875-0009839 to -0009849)
  - Revised Purified water system layout (APL-MDL 2875-0009872)
  - SOP on preparation of drawings (APL-MDL 2875-0009852 to -0009855)
  - Work order number and list of equipments with status of gaskets changed (APL-MDL 2875-0009828 to -0009838)

- Cover Letter dated March 12, 2013, and EIR for June 4-8, 2012, Inspection of Unit XI (APL-MDL 2875-0009856 to -0009871)
- FDA Form 483 for June 4-8, 2012, Inspection of Unit XI (APL-MDL 2875-0009850 to -0009851)
- Aurobindo First Update to USFDA 483 Observations from Inspection of Unit XI Dates February 4-9, 2019
  - Summary of Correction and Preventative Actions (APL-MDL 2875-0029335 to -0029348)
- Update to FDA Inspection Responses for Unit XI (APL-MDL 2875-0000129 to -0000342)
  - Attachment I Training Records (APL-MDL 2875-0000448 to -0000453)
  - Attachment II Report on Comprehensive Review of GC Methods (APL-MDL 2875-0000600 to -0000621)
  - Attachment III Report on GC Methods Related to Recovered Solvents (APL-MDL 2875-0000431 to -0000447)
  - Attachment IV Report on Review of Method Validations and Method Transfers (APL-MDL 2875-0000526 to -0000590)
  - Attachment V Status Report on BPCR revision for handling of discharge (APL-MDL 2875-0000622 to -0000818)
  - Attachment VI (APL-MDL 2875-0000515 to -0000525)
  - Attachment VII Valsartan Process II Investigation Report (APL-MDL 2875-0000343 to -0000430)
  - Attachment VIII Interim Report on Testing of Raw Materials, Report on Cleaning Validation (APL-MDL 2875-0000454 to -0000514)

- Attachment IX IQ and OQ Report for Glass Line Reactor GLJ007 (APL-MDL 2875-0000591 to -0000599)

- Aurobindo USFDA Initial Response to Form 483
  - Cover Letter dated March 4, 2019 (APL-MDL 2875-0030573 to -0030629)
  - Annexure 1A-1: Investigation Report to determine the source and nature of the unknown peaks observed during residual solvent analysis in Valsartan API using GC methods (APL-MDL 2875-0030846 to -0030935)
  - Annexure 1A-2: Investigation Report to determine the source and nature of the unknown peaks using GC method observed in the Recovered ethyl acetate of Valsartan (APL-MDL 2875-0030800 to -0030831)
  - Annexure 1A-3: GC-MS Data of Unknown Peaks in RS Methods of Valsartan (APL-MDL 2875-0030832 to -0030845)
  - Annexure 1A-5: Ethyl Propionate Safety Data (APL-MDL 2875-0030681 to -0030682)
  - Annexure 1A-6: GC-MS Data of Recovered Ethyl Acetate (APL-MDL 2875-0030661 to -0030680)
  - Annexure 1A-7: Revised Valsartan Release Specification STP (APL-MDL 2875-0030682 to -0030784)
  - Annexure 1A-9: Specification & STP of Recovered Ethyl Acetate pH adjusted at 2-2.5 (APL-MDL 2875-0030785 to -0030792)
  - Annexure 1A-9: Specification STP of Recovered Ethyl Acetate Stage IA (APL-MDL 2875-0030793 to -0030799)
  - Annexure 1C-1: Trend data of acetic acid (APL-MDL 2875-0030936)
  - Annexure 1C-2: PDE Calculation of valeric acid (APL-MDL 2875-0030937)
  - Annexure 1C-4: Valsartan revised US regulatory Specification and STP (APL-MDL 2875-0030938 to -0030991)
  - Annexure 1D-1: Standard Testing Procedure for Tin content (APL-MDL 2875-0030652 to -0030659)
  - Annexure 1D-2: Analytical Method Validation Report (APL-MDL 2875-0030630 to -0030651)

- Annexure 1D-3: Trend Data of Tin Content (APL-MDL 2875-0030660)
- Annexure: 1E1-1: LCMS Method Validation Report (APL-MDL 2875-0031006 to -0031056)
- Annexure 1E1-2: Test procedure for NDMA and NDEA contents in API (APL-MDL 2875-0030992 to -0030998)
- Annexure 1E1-3: Method Suitability Report (APL-MDL 2875-0030999 to -0031005)
- Annexure 1E1-4: Determination of NDMA and NDEA Content in Valsartan Water Samples (APL-MDL 2875-0031057 to -0031063)
- Annexure 1E2-1: Validation of Head Space-GCMS Method for the Determination of NDMA and NDEA Contents in Valsartan Drug Substance (APL-MDL 2875-0031108 to -0031151)
- Annexure 1E2-3: Verification of Head Space-GCMS Method for the Determination of NDMA and NDEA Contents in Different Crossover Products (APL-MDL 2875-0031064 to -0031085)
- Annexure 1E2-6: Verification of Head Space-GCMS Method for the Determination of NDMA and NDEA Contents in Different Crossover Products, Solvents and Reagents (APL-MDL 2875-0031086 to -0031107)
- Annexure 2A-1: Brief manufacturing process and synthetic route, Olmesartan Medoxomil (APL-MDL 2875-0030344 to -0030348)
- Annexure 2A-2: Validation of Head Space GC-MS method for determination of NDMA and NDEA in Olmesartan Medoxomil (APL-MDL 2875-0030386 to -0030453)
- Annexure 2A-3: Olmesartan Medoxomil, NDMA, NDEA testing results (APL-MDL 2875-0030503 to -0030514)
- Annexure 2A-4: Olmesartan Medoxomil API specification with limit ‘Should be Not Detected’ for NDMA and NDEA (APL-MDL 2875-0030332 to -0030338)
- Annexure 2A-5: KSM-Route of Synthesis (APL-MDL 2875-0030339 to -0030343)
- Annexure 2A-6: Bromoethyl Biphenyl Trityl Tetrazole (Tetrazole compound): Method Verification Report (APL-MDL 2875-0030454 to -0030498)
- Annexure 2A-7: Specification and Test Method for Bromoethyl Biphenyl Trityl Tetrazole (Tetrazole compound) & Analytical method validation (APL-MDL 2875-0030349 to -0030385)

- Annexure 2A-8: Information received from KSM vendors (APL-MDL 2875-0030499 to -0030502)

- Annexure 2A-9: Specification and Test Method for 4-(1-Hydroxy-1-Methylethyl)-2-Propylimidazole-5-Carboxylic Acid Ethyl Ester [Imidazole derivative] and 4-Chloromethyl-5-Methyl-1,3-Dixol-2-One & Method validation report of Imidazole derivative (APL-MDL 2875-0030515 to -0030572)

- Annexure 2B-1: Protocol 'GENP/JV/18/022' (APL-MDL 2875-0030325 to -0030331)

- Annexure 2B-2: Method Verification Report for Determination of contents o NDMA and NDEA in Valsartan Cleaning Samples (APL-MDL 2875-0029772 to -0029814)

- Annexure 2B-3: 'GENP/OV-I/19/012' Protocol for Re-assessment on Cleaning Validation of Valsartan Manufacturing Equipment (APL-MDL 2875-0029815 to -0030031)

    - Annexure 2B-3 (Pages 24-29) (APL-MDL 2875-0030040 to -0030045)

- Annexure 2B-4: Risk Assessment Report 'GENR/WR-I/18/023', Investigation Report 'GENI/WR-I/18/023' (APL-MDL 2875-0029653 to -0029771)

- Annexure 2B-5: SOP KQA 026, "Manufacturing Equipment Cleaning Validation Policy" (APL-MDL 2875-0029561 to -0029652)

- Annexure 2B-6: Protocol and Report for Establishment of Swab sampling Locations, Protocol- 'GENP/CVSL/19/005' and Report- 'GENR/CVLS/19/005' (APL-MDL 2875-0030279 to -0030301)

- Annexure 2B-7: 'GENP/JV-I/19/010', Specific Cleaning Procedure for SRJ014 (APL-MDL 2875-0030046 to -0030057)

- Annexure 2B-8: SOP KMF073 Rev- 'Cleaning Procedure for Reactor' (APL-MDL 2875-0030058 to -0030278)

- Annexure 2B-9: Deviation Investigation Report (APL-MDL 2875-0030302 to -0030324)

- Annexure 2B-10: Revised the specifications for the presence of NDMA and NDEA impurity residues in Valsartan Drug Substance (APL-MDL 2875-0030032 to -0030039)

- Annexure 3-1: Copy of the executed BPCR # KBBKA102 Rev-01 Stage-I, steps No. 15.1.5 and 15.2.5 (APL-MDL 2875-0029512 to -0029547)

- Annexure 3-2: Copy of the revised BPCR # KBBKA102, REV-02, Stage-I, steps No. 15.1.5 and 15.2.5 (APL-MDL 2875-0029466 to -0029501)

- Annexure 3-3: Copy of revised SOP KMF029 and formats #KNF029-F03-00, #KMF029-F04-00 (APL-MDL 2875-0029548 to -0029560)

- Annexure 3-4: Copy of revised BPCRs of other stages (Stage II & API_ of Olmesartan, KBFKAII03-REV-03, KBAKAIII01, REV-03 (APL-MDL 2875-0029354 to -0029465)

- Annexure 3-5: Training Records on Olmesartan BPCR revisions and revision of SOP KMF029 (APL-MDL 2875-0029502 to -0029511)

- FDA Form 483 for Inspection dates February 4-9, 2019 (Unit XI)

- Letter to FDA dated August 9, 2019 re: Update Response to FDA Warning Letter 320-19-27 submitted for Aurobindo Pharma Ltd. Unit XI (FEI 3004611182) (APL-MDL 2875-0009812)

    - Attachment -1 Quality Improvement Plan (QIP) (APL-MDL 2875-0009813 to -0009820)

- FDA Warning Letter 320-19-27 to Unit XI dated June 20, 2019 (APL-MDL 2875-0009806 to -0009811)

- Initial Response to Warning Letter 320-19-27 (July 15, 2019)

    - Cover Letter (APL-MDL 2875-0002345 to -0002346)

    - Response to WL 320-19-27 (APL-MDL 2875-0004189 to -0004261)

    - Summary of Corrective and Preventative Actions that are Implemented or Under Implementation (APL-MDL 2875-0004183 to -0004188)

    - Observation 1

        - Attachment -1 Assessment report on Valsartan Process-II [For presence of N-Nitrosodiethylamine (NDEA) impurity (APL-MDL 2875-0003745 to -0003756)

        - Attachment -2 Summary of Recalls for Valsartan API (APL-MDL 2875-0003719 to -0003732)

- Attachment -3 Valsartan investigation report (APL-MDL 2875-0003498 to -0003713)
- Attachment -4 Olmesartan Medoxomil risk assessment report (APL-MDL 2875-0003469 to -0003497)
- Attachment -5 Valsartan, o-Xylene route Specification with inclusion of 'other nitrosamine test' (APL-MDL 2875-0003733 to -0003744)
- Attachment -6 NDMA and NDEA testing results of materials sourced from 'Lantech Pharmaceuticals Ltd' (APL-MDL 2875-0003714 to -0003718)

o Observation 1.1

- Attachment -7 Vendor Management SOPs
  - Evaluation of External Vendor for raw materials (ZQA016) (APL-MDL 2875-0002679 to -0002815)
  - Qualification, Evaluation of Internal Vendor for Raw Material (ZQA017) (APL-MDL 2875-0002384 to -0002457)
  - Vendor Audit Management Procedure (ZQA018) (APL-MDL 285-0002590 to -0002678)
  - Qualification of Logistic Service Provider (LSP) for Transportation of Solvent (ZQA046) (APL-MDL 2875-0002458 to -0002478)
  - Selection, Approval and evaluation of CMU (ZQA047) (APL-MDL 2875-0002479 to -0002589)

o Observation 1.2

- Attachment -08 NMBA Test results of Valsartan API (APL-MDL 2875-0003024 to -0003025)
- Attachment -09 Test results of 'other nitrosamines' for the Valsartan & Olmesartan API batches manufactured within 2018-2019; results available till date (APL-MDL 2875-0003307 to -0003324)
- Attachment -10 Addendum to investigation report on N-Nitrosamine Impurities {N-Nitrosodimethylamine (MDMA) and (N-Nitrosodiethylamine (NDEA)} (APL-MDL 2875-0003242 to -0003306)
- Attachment -11 Risk assessment (APL-MDL 2875-0003026 to -0003233)

- Attachment -12 Testing results of KSM/reagent/API related to 'non-sartan' products (APL-MDL 2875-0003234 to -0003241)

- Observation 1.3

  - Attachment -13 Test Results of 'NDMA' & "NDEA' for Valsartan & Olmesartan Medoxomil API (APL-MDL 2875-0002816 to -0002855)

  - Attachment -14 Test results of 'mutagenic impurities' for Valsartan and Olmesartan Medoxomil (APL-MDL 2875-0002856 to -0002950)

- Observation 1.4

  - Attachment -15 Valsartan API method equivalence report for NDMA and NDEA testing by LC-MS/MS and GC/MS-Headspace method (APL-MDL 2875-0002365 to -0002383)

  - Attachment -16 Assessment report on chromatographic data of Valsartan batches to check whether any unexpected Nitrosamines impurity peaks are present (APL-MDL 2875-0002347 to -0002364)

- Observation 1.5

  - Attachment -17 List of products where major changes have been made and the DMF amendments have been filed (APL-MDL 2875-0004177 to -0004180)

  - Attachment -18 Risk assessment reports of PGI for 'sartan' products (APL-MDL 2875-0003757 to -0003908)

  - Attachment -19 Risk assessment reports of PGI for 'non-sartan' products (APL-MDL 2875-0003909 to -0004176)

  - Attachment -20

  - Attachment -21 Subject Matter Expert Report on procedures and strategy adopted by Aurobindo Pharma Limited API Research Centre to conduct risk assessment for n-nitrosamines and mutagenic impurities (APL-MDL 2875-0004181 to -0004182)

- Observation 2.1

  - Attachment -22 Protocol for Inspection of Manufacturing equipment (APL-MDL 2875-0002951 to -0003012)

- Observation 2.2

        - Attachment -23 Protocol for the Evaluation of Equipment Suitability (APL-MDL 2875-0003013 to -0003023)

    - Observation 3

        - Attachment -24 Valsartan API Specification (APL-MDL 2875-0003379 to -0003436)

        - Attachment -25 Retrospective Review report of Acetic Acid and Valeric Acid Content in Valsartan API (APL-MDL 2875-0003349 to -0003378)

        - Attachment -27 SOP ZQA038 Identification and Reporting of Unknown peaks in Gas Chromatography analysis (APL-MDL 2875-0003437 to -0003468)

        - Attachment -28 Summary of Unknowns observed in Gas chromatographic analysis of active pharmaceutical ingredient (API) (APL-MDL 2875-0003336 to -0003348)

        - Attachment -29 Protocol for Independent Assessment of Overall system for investigating unknown peaks, deviations, discrepancies, out of specifications results, complaints, other failures and retrospective review of all distributed batches within expiry date (APL-MDL 2875-0003325 to -0003335)

- First Update on Response to USFDA WL 320-19-27 (July 20, 2019)

    - Cover Letter (APL-MDL 2875-0009662 to -0009664)
    - Attachment -1 Risk assessment reports of PGI for non-sartan Products (APL-MDL 2875-0009665 to -0009805)

- Second Update on Response to USFDA WL 320-19-27 (September 5, 2019)

    - Cover Letter (APL-MDL 2875-0002338 to -0002344)

    - Status Update for Corrective Actions (Implemented/In Progress) (APL-MDL 2875-0002330 to -0002337)

    - Attachment -1 Test Results of Valsartan API (Process II, Toluene Route) for ‘Other Nitrosamines’ (APL-MDL 2875-0001664 to -0001689)

    - Attachment -2 Test Results of Valsartan API (Process II, o-Xylene Route) for ‘Other Nitrosamines’ (APL-MDL 2875-0002036 to 0002039)

- Attachment -3 Test Result of Olmesartan Medoxomil API for 'Other Nitrosamines' (APL-MDL 2875-0002089 to -0002094)

- Attachment -4 Analytical Method Validation of 'Other Nitrosamines' Test for KSM Used in Valsartan Process (APL-MDL 2875-0002226 to -0002284)

- Attachment -5 Analytical Method Validation of 'Other Nitrosamines' Test for KSM Used in Olmesartan Medoxomil Process (APL-MDL 2875-0001809 to -0001868)

- Attachment -6 Revised Specification for Olmesartan Medoxomil by Including the Limits for 'Other Nitrosamines' [Limit: Should be 'Not Detected'] (APL-MDL 2875-0002098 to -0002108)

- Attachment -7 Disposal Details of Recovered Tri N Butyl Tin Chloride (TNBTC) Received from Lantech Pharmaceutical Pvt Ltd (CMU) (APL-MDL 2875-0001799 to -0001808)

- Attachment -8 Disposal Details of Recovered 2,6-Lutidine Received from JPR Laboratories Pvt Ltd (CMU) (APL-MDL 2875-0001869 to -0001875)

- Attachment -9 Test Results of CAB Propane Samples for NDMA and NDEA (APL-MDL 2875-0001796 to -0001798)

- Attachment -10 Test Results of 'Other Nitrosamines' for Valsartan API Batches Extended Back from May 2019 to June 2017 (All the Batches Currently Available in US Market) (APL-MDL 2875-0001967 to -0001968)

- Attachment -11 Revised Specifications for Valsartan KSMs (APL-MDL 2875-0002079 to -0002088)

- Attachment -12 Withdrawal of US DMF for the Valsartan TTBB Route (APL-MDL 2875-0002095 to -0002097)

- Attachment -13 Test Results of 'Other Nitrosamines' for Olmesartan Medoxomil API Batches Extended Back from May 2019 to June 2017 (All the Batches Currently Available in US Market) (APL-MDL 2875-0002040 to -0002041)

- Attachment -14 Test Results of 'NMBA' Impurity Content for Olmesartan Medoxomil (APL-MDL 2875-0001969 to -0001973)

- Attachment -15 Revised Specifications for Olmesartan Medoxomil KSMs (APL-MDL 2875-0002056 to -0002076)

- Attachment -16 Test Results of KSM/API/Reagent Samples Related to Non-Sartan Products (APL-MDL 2875-0002109 to -0002136)

- Attachment -17 Revised Specifications for KSM/API/Reagents Based on Action Points Derived from Nitrosamine Evaluation of 'Non-ARBS/Non-Sartans' (APL-MDL 2875-0001876 to -0001966)

- Attachment -18 Introduction of Process Controls 'Non ARB/Non-Sartan' Products (APL-MDL 2875-0001974 to -0001999)

- Attachment -19 Revised Specification for Valsartan and Olmesartan Medoxomil API by Including Mutagenic Impurities (APL-MDL 2875-0002000 to -0002035)

- Attachment -20 Assessment of Potential Genotoxic Impurities [PGI] in 'Non-ARB/Non-Sartan' Products (APL-MDL 2875-0002137 to -0002225)

- Attachment -21 Revised SOP KQC006 on "Preparation, Review, Approval, Distribution, Revision and Retrieval of Specifications and Standard Testing Procedures' (APL-MDL 2875-0002042 to -0002055)

- Attachment -22 Status on Testing of 30 Consecutive Incoming Raw Material and Solvent Batches to Confirm Absence of Nitrosamine Impurities (APL-MDL 2875-0001782 to -0001795)

- Attachment -23 Status Update on Inspection of Manufacturing Equipment & Evaluation of Equipment Suitability (APL-MDL 2875-0002077 to -0002078)

- Attachment -24 Statement on DMF's Amendment Based on the Evaluation on Alignment of Regulatory and Release Specifications (APL-MDL 2875-0001690 to -0001780)

- Attachment -25 Evaluation Report on GC Unknown Impurity (APL-MDL 2875-0002285 to -0002329)

- Third Update on Response to USFDA WL 320-19-27 (October 15, 2019)

  - Cover Letter (APL-MDL 2875-0001656 to -0001663)

  - Status on USFDA Warning Letter Corrective and Preventative Actions (Implemented/Ongoing) (APL-MDL 2875-0001648 to -0001655)

  - Attachment – 1 Status on Testing of 30 Consecutive Incoming Raw Material and Solvent Batches to Confirm Absence of Nitrosamine Impurities (APL-MDL 2875-0001626 to -0001647)

- Attachment – 2 Analytical Method Development and Method Validation of 'Other Nitrosamines' Test for Fresh Solvents Used in Valsartan Process (APL-MDL 2875-0001386 to -0001567)
- Attachment – 3 Analytical Method Development and Method Validation of 'Other Nitrosamines' Test for Other Raw Materials Used in Valsartan Process (APL-MDL 2875-0001054 to -0001198)
- Attachment – 4 Analytical Method Development and Method Validation of 'Other Nitrosamines' Test for Fresh Solvents Used in Olemsartan Medoxomil Process (APL-MDL 2875-0001206 to -0001385)
- Attachment – 5 Analytical Method Development and Method Validation of 'Other Nitrosamines' Test for Other Raw Materials Used in Olmesartan Medoxomil Process (APL-MDL 2875-0000819 to -0000963)
- Attachment – 6 Testing of KSM/API/Reagent Samples Related to Non-Sartan Products (APL-MDL 2875-0001027 to -0001053)
- Attachment – 7 Status Update on Inspection of Manufacturing Equipment & Evaluation of Equipment Suitability (APL-MDL 2875-0001199 to -0001202)
- Attachment – 8 Engagement of a Third-Party Consulting Firm to Conduct a Comprehensive, On-Site Assessment of the API Equipment Maintenance and Cleaning Program (APL-MDL 2875-0001575 to -0001625)
- Attachment – 9 Formation of a Site-Based, Cross-Functional Equipment Maintenance Team (EMT) Including Site and Corporate QA and Engineering to Assess the Outcomes of the Third-Party Assessments (APL-MDL 2875-0001203 to -0001205
- Attachment – 10 DMF's Amended to Include Additional Testing Controls (APL-MDL 2875-0001568 to -0001574)
- Attachment – 11 Evaluation Report on GC Unknown Impurity (APL-MDL 2875-0000964 to -0001026)

- Fourth Update on Response to USFDA WL 320-19-27 (November 15, 2019)
  - Cover Letter (APL-MDL 2875-0009650 to -0009661)
  - Status on USFDA Warning Letter Corrective and Preventative Actions (Implemented/Ongoing) (APL-MDL 2875-0004262 to -0004270)

- Attachment -1 Status on Testing of 30 Consecutive Incoming Raw Material and Solvent Batches to Confirm Absence of Nitrosamine Impurities (APL-MDL 2875-0006333 to -0006363)

- Attachment -2 Risk Assessment Reports on Nitrosamine Impurities: “Tramadol Hydrochloride, Pioglitazone Hydrochloride and Zidovudine” (APL-MDL 2875-0008850 to -0008940)

- Attachment -3a Potential Genotoxic Impurities (PGI) Control Strategy for Non-Sartan Products (APL-MDL 2875-0005640 to -0005968)

- Attachment -3b PGI Assessments and Controls (APL-MDL 2875-0004271 to -0004551)

- Attachment -3c PGI Assessments and Controls (APL-MDL 2875-0005969 to -0006241)

- Attachment -4 Potential Genotoxic Impurities (PGI) Assessment Reports of Non-Sartan Products (of Other Aurobindo API Units) (APL-MDL 2875-0007333 to -0007552)

- Attachment -5 Report on Inspection of Manufacturing Equipment (APL-MDL 2875-0006528 to -0006752)

- Attachment -6 Report on Evaluation of Equipment Suitability (APL-MDL 2875-0006242 to -0006319)

- Attachment -7 The EMT Works on Outcome of the Protocols (Inspection of Manufacturing Equipment & Evaluation of Equipment Suitability) (APL-MDL 2875-0006320 to -0006332)

- Attachment -8 Aurobindo Pharma Ltd. (APL) Corporate Level Equipment Maintenance Team (APL-MDL 2875-0006364 to -0006366)

- Attachment -9 New Engineering Standards for Equipment, Policies on Cleaning Processes, Policies on Cleaning Processes, Clean-In-Place & Clean-Out-Of-Place Systems (APL-MDL 2875-0008372 to -0008537)

- Attachment -10 Subject Matter Experts in Pharmaceutical Equipment Qualification, Cleaning and Maintenance (APL-MDL 2875-0008019 to -0008039)

- Attachment -11a Unknown Impurity Evaluation (APL-MDL 275-0008941 to -0009207)

- Attachment -11b Unknown Impurity Evaluation (APL-MDL 2875-0009208 to -0009496)
- Attachment -11c Unknown Impurity Evaluation (APL-MDL 2875-0004552 to -0004870)
- Attachment -11d Unknown Impurity Evaluation (APL-MDL 2875-0006939 to -0007332)
- Attachment -11e Unknown Impurity Evaluation (APL-MDL 2875-0008048 to -0008371)
- Attachment -11f Unknown Impurity Evaluation (APL-MDL 2875-0008538 to -0008849
- Attachment -11g Unknown Impurity Evaluation (APL-MDL 2875-0007727 to -0008018)
- Attachment -11h Unknown Impurity Evaluation (APL-MDL 2875-0004883 to -0005176)
- Attachment -11i Unknown Impurity Evaluation (APL-MDL 2875-0005177 to -0005496)
- Attachment -12 Independent Assessment on Overall System for Investigation Unknown Peaks, Deviations, Discrepancies, OOS Results, Complaints, Other Failures and Retrospective Review of All Distributed Batches within Expiry Date (APL-MDL 2875-0006753 to -0006938)
- Attachment -13 Remediation Plan of Outcome of Independent Assessment of Overall System (APL-MDL 2875-0008040 to -0008047)
- Attachment -14a Interim Report on Evaluation of Equipment Cleaning Procedure (APL-MDL 2875-0006367 to -0006527)
- Attachment -14b Evaluation on Equipment Cleaning Procedure (APL-MDL 2875-0009497 to -0009649)
- Attachment -14c Evaluation on Equipment Cleaning Procedure (APL-MDL 2875-0005497 to -0005639)
- Attachment -14d Evaluation on Equipment Cleaning Procedure (APL-MDL 2875-0007553 to -0007726)

  - Attachment -15 Summary on DMF Amendments (APL-MDL 2875-0004871 to -0004882)

- Unit XI USFDA Audit Details (APL-MDL 2875-0009873)

- Note on Investigation into the Cause of Nitrosamine Carryover, Controls in Place (APL-MDL 2875-0023250 to -0023273)

  - Risk Assessment and Investigation Reports (APL-MDL 2875-0023509 to -0023626)

  - Valsartan Final Investigation Report (APL-MDL 2875-0023627 to -0023841)

  - Olmesartan Risk Assessment Report (APL-MDL 2875-0023842 to -0023866)

  - Addendum to Olmesartan Risk Assessment Report (APL-MDL 2875-0023481 to -0023508)

  - Assessment of Non Sartan APIs (APL-MDL 2875-0023274 to -0023480)

- Unit XI Summary of Recalls for Valsartan API

- APL Healthcare Unit-I

  - FDA Form 483 Observations for Inspection dates March 27-31, 2017 (APL-MDL 2875-0028792 to -0028797)

  - Cover Letter & EIR for Inspection dates March 27-31, 2017 (APL-MDL 2875-0009940 to -0009966)

  - Response to US FDA 483 Observations for Inspection dates March 27-31, 2017 (dated April 19, 2017) (APL-MDL 2875-0028206 to -0028791)

  - 483 Observations for December 17-21, 2018 Inspection (APL-MDL 2875-0028920 to -0028923)

  - EIR for December 17-21, 2018 Inspection (APL-MDL 2875-0028798 to -0028821)

  - Response to US FDA 483 Observations for December 2018 Inspection (January 9, 2019) (APL-MDL 2875-0028822 to -0028919)

- APL Unit-III

  - Response to Warning Letter 320-11-013 (dated June 11, 2011) (APL-MDL 2875-0028148 to -0028178)

- Form 483 Observations June 2015 Inspection (APL-MDL 2875-0028065 to -0028067)
- Response to US FDA 483 Observations from June 18-26, 2015, Inspection (July 15, 2015) (APL-MDL 2875-0009874 to -0009939 & APL-MDL 2875-0028041 to -0028064)
- Response to US FDA Form 483 Observations from April 10-18, 2017, Inspection (May 8, 2017) (APL-MDL 2875-0026164 to -0026485)
- Response to US FDA Form 483 Observations from May 13-24, 2019 Inspection (APL-MDL 2875-0026486 to -0027963)
- EIR for January 25-29, 2016, Inspection (APL-MDL 2875-0026099 to -0026113)
- EIR for April 10-18, 2017, Inspection (APL-MDL 2875-0026114 to -0026159)
- 483 Observations April 2017 Inspection (APL-MDL 2875-0026160 to -0026163)
- EIR for May 13-24, 2019, Inspection (APL-MDL 2875-0027979 to -0028040)
- 483 Observations May 2019 Inspection (APL-MDL 2875-0027964 to -0027978)
- EIR for June 2015 Inspection (APL-MDL 2875-0028068 to -0028123)
- EIR for February 2012 Inspection (APL-MDL 2875-0028124 to -0028147)

- APL Unit-VII
  - EIR Inspection Dates March 5-13, 2016 (APL-MDL 2875-0026081 to -0026098)
  - EIR January 25-29, 2016 Inspection (APL-MDL 2875-0023872 to -0023902)
  - Form 483 January 2016 Inspection (APL-MDL 2875-0023867 to -0023871)
  - Response to FDA 483 Observations from January 2016 Inspection (APL-MDL 2875-2288525 to -2288826)
  - Form 483 September 2019 Inspection (APL-MDL 2875-0024066 to -0024079
  - Response to US FDA 483 Observations from September 19-27, 2019, Inspection (APL-MDL 2875-0023903 to -0024065)
    - Attachment 1.1 General CAPAs implemented since Jan 2017 (APL-MDL 2875-0024451 to -0024460)

- Attachment 1.2 Independent Assessment of Invalid Out of Specification Investigations by subject matter expert(s) [SME] from Aurobindo corporate quality (APL-MDL 2875-0024644 to -0024652)

- Attachment 1.3 'Independent Assessment of Invalid Out of Specification Investigations by independent subject matter expert from Meridan consulting' report (APL-MDL 2875-0026021 to -0026027)

- Attachment 1.4 Stability data of batch which are with in expiry and having subsequent stability test points data (not subjected for retesting) (APL-MDL 2875-0024335 to -0024338)

- Attachment 1.5 Report for re-testing of Products Involved in Invalid Out of Specification Investigations (excluding currently expired, and stability study batches having subsequent test points (APL-MDL 2875-0024830 to -0024891)

- Attachment 1.6 Report for re-testing of Products Involved in Invalid Out of Specification Investigations (excluding currently expired, and stability study batches having subsequent test points) witnessed by subject matter expert from Meridan consulting (APL-MDL 2875-0025236 to -0025316)

- Attachment 1A.1 Training record of analysts (importance of accurate documentation in all tests performed, to include hypothesis testing) (APL-MDL 2875-0024699 to -0024703)

- Attachment 1B.1 pH Meter (PHMB0001) Log pages (APL-MDL 2875-0024826 to -0024829)

- Attachment 1B.2 Addendum investigation report (APL-MDL 2875-0024653 to -0024690)

- Attachment 1B.3 Retraining record (APL-MDL 2875-0024793 to -0024794)

- Attachment 1B.4 Stability data of exhibit batches and commercial batches (APL-MDL 2875-0024787 to -0024790)

- Attachment 1D.1 Revised SOP FU7-PR-GEN-01 1 "Procedure for Handling of Rejects in Packing" (APL-MDL 2875-0024892 to -0024928)

- Attachment 1E.1 Interim Re-Investigation Report No. APL-FU7-2019-USA-PCM-00982 (APL-MDL 2875-0024205 to -0024228)

- Attachment 1F.1 Failure Investigation Report APL Unit07/INV/044/19-00 (APL-MDL 2875-0024495 to -0024602)

- Attachment 2A.1 Batch details of Dutasteride and Tamsulosin Hydrochloride Capsules 0.5 mg and 0.4 mg, dated 20-Sep-2019 (APL-MDL 2875-0024461 to -0024462)

- Attachment 2A.2 Batch details of Dutasteride and Tamsulosin Hydrochloride Capsules 0.5 mg and 0.4 mg, dated 23-Sep-2019 (APL-MDL 2875-0024791 to -0024792)

- Attachment 2A.3 Laboratory Investigation for OOS numbers QCOOS16087, QCOOS16088, QCOOS16089, QCOOS16090 and QCOOS16094 (APL-MDL 2875-0024319 to -0024334)

- Attachment 2B.1 SOP CQA-CP-GEN-005 Version 3.0.0.0 "Operation of DMS by the User" (APL-MDL 2875-0024288 to -0024318)

- Attachment 2B.2 DMS Manager and Publisher Details (APL-MDL 2875-0024400 to -0024402)

- Attachment 2B.3 MS PDMS Audit Details (APL-MDL 2875-0024955 to -0024956)

- Attachment 2B.4 CQA-CP-GEN-046 Version 7.0.0.0 "Preparation, Approval, Authorization and Control of Batch Processing an Packing Records" (APL-MDL 2875-0024742 to -0024786)

- Attachment 2B.5 Independent Assessment Protocol for the reconciliation of batch records (APL-MDL 2875-0024737 to -0024741)

- Attachment 2B.6 Independent Assessment Report for the reconciliation of batch records (APL-MDL 2875-0024433 to -0024436)

- Attachment 2B.7 Assessment Report to evaluate each of the 145 entries in the Excel Sheet "DMS Copy Re-Issuance" (APL-MDL 2875-0024463 to -0024467)

- Attachment 2B.8 SOP FU7-QA-GEN-002 Version 7.0.0.0, Effective from 19-Oct-2019 (APL-MDL 2875-0025082 to -0025091)

- Attachment 2B.9 Training Records (APL-MDL 2875-0024397 to -0024399)

- Attachment 2B.10 Revised SOP CQA-CP-GEN-005 Version 4.0.0.0 "Operation of DMS by the User" (APL-MDL 2875-0024704 to -0024736)

- Attachment 3A.1 ProcessPad Implementation Schedule (APL-MDL 2875-0024691 to -0024698)

- Attachment 3A.2 Protocol FU7-UNIT VII-ACQP-0116, Protocol for Retrospective Assessment of Product Quality for all commercially distributed US Products (APL-MDL 2875-0024973 to -0024997)

- Attachment 3A.3

    - Retrospective Assessment Review Report Loperamide Hydrochloride Tablets (APL-MDL 2875-0025957 to -0025980)

    - Retrospective Assessment Review Report Rabeprazole Sodium Delayed Release Tablets (APL-MDL 2875-0025888 to -0025914)

    - Retrospective Assessment Review Report Fexofenadine Hydrochloride and Pseudoephedrine Hydrochloride Extended Release Tablets (APL-MDL 2875-0025915 to -0025956)

    - Retrospective Assessment Review Report Minocycline Hydrochloride Extended Release Tablets USP 55mg, 65mg, 80mg, 105mg (APL-MDL 2875-0025641 to -0025708)

    - Retrospective Assessment Review Report Desogestrel and Ethinyl Estradiol Tablet, & Ethinyl Estradiol Tablets, Inert Tablets of Desogestrel and Ehtinyl Estradiol Tablets (APL-MDL 2875-0025709 to -0025749)

    - Retrospective Assessment Review Report Glipizide Extended-Release Tablets (APL-MDL 2875-0025805 to -0025887)

    - Retrospective Assessment Review Report Norethindrone Acetate and Ethinyl Estradiol Tablets USP 1mg/20mcg & Ferrous Fumarate Tablets USP 75mg (APL-MDL 2875- 0025495 to -0025543)

    - Retrospective Assessment Review Report Desogestrel and Ethinyl Estradiol Tablets & Inert Tablets of Desogestrel and Ethinyl Estradiol Tablets (APL-MDL 2875-0025981 to -0026020)

    - Retrospective Assessment Review Report Norgestimate and Ethinyl Estradiol Tablets, USP 0.180 mg/0.035mg 0.215mg/0.035mg and 0.250mg/0.035mg & Inert Tablets for Norgestimate and Ethinyl Estradiol Tablets (APL-MDL 2875-0025544 to -0025640)

    - Retrospective Assessment Review Report Olmesartan Medoxomil Tablets (APL-MDL 2875-0025750 to -0025804)

  - Retrospective Assessment Review Report Guaifenesin and Dextromethorphan HBr Extended Release Tablets (APL-MDL 2875-0025359 to -0025494)

- Attachment 3A.4 Reports for Retrospective Assessment of Product Quality for 2 US Products Indicated in Phase 2 (APL-MDL 2875-0025108 to -0025235)

- Attachment 3B.1 Summary of Retrospective review of three product batches with longest hold time along with reports of retrospective assessments of Hold Time for Product with longest hold time (APL-MDL 2875-0024998 to -0025081)

- Attachment 4.1 Revised of SOP FU7-QC-GEN-047 title "Reporting and Review of Work Sheet" (APL-MDL 2875-0024929 to -0024954)

- Attachment 4.2 SOP FU7-QA-GEN-080, "Review Procedure for Analytical Data" (APL-MDL 2875-0024960 to -0024972)

- Attachment 4.3 Revised of SOP FU7-QC-GEN-0102 title "Audit Trail Review and Management of Laboratory Software" (APL-MDL 2875-0024229 to -0024282)

- Attachment 4.4 'Report for Independent Assessment of audit trail / events review in Tiamo Software of Unit-VII' by subject matter expert from corporate quality (APL-MDL 2875-0025317 to -0025356)

- 4.5 Report of an independent assessment by Meridan Consulting to evaluate and confirm Aurobindo's audit trail assessment and findings accuracy and witness the selected samples from the "Determination Error" category for retesting (APL-MDL 2875-0024171 to -0024192)

- Attachment 5A.1 SOP FU7-QC-GEN-036, Version 4.0.0.0, "Aberrant Results" (APL-MDL 2875-0024795 to -0024815)

- Attachment 5B.1 Process Non-conformance Reference # APL-FU7-PNC-19-4494 (APL-MDL 2875-0024403 to -0024429)

- Attachment 5D.1 Evaluation Report of the Product Samples observed in Documentation Room 1 on 19-Sep-2019 (APL-MDL 2875-0024126 to -0024170)

- Attachment 5E.1 Evaluation Report of 254 Batch Records observed in Document Cabinet labeled "Waiting for COA" in the IPQA Packing Room (APL-MDL 2875-0024957 to -0024959)

- Attachment 5E.2 Evaluation of Batch Records available in IPQA office on 19-Sep-2019 (APL-MDL 2875-0024339 to -0024396)
- Attachment 5E.3 Training Record (APL-MDL 2875-0025357 to 0025358)
- Attachment 5F.1 SOP FU7-QC-GEN-047, "Reporting and Review of Work Sheet" (APL-MDL 2875-0024468 to -0024492)
- Attachment 5F.2 SOP CQA-CP-QCCI-GEN-0005, "Chromatography Data Review in Empower-3 Chromatography Software" (APL-MDL 2875-0024603 to -0024641)
- Attachment 5F.3 SOP FU7-QA-GEN-080, "Review Procedure for Analytical Data" (APL-MDL 2875-0025092 to -0025104)
- Attachment 5F.4 SOP FU7-QC-GEN-0102, "Audit Trail Review and Management of Laboratory Software" (APL-MDL 2875-0026028 to -0026080)
- Attachment 5G.1 Process Non-conformance Reference # APL-FU7-PNC-19-4783 (APL-MDL 2875-0025105 to -0025107)
- Attachment 6.1 Page # 21 of Pam Glatt Instruction manual for FBE-250C (APL-MDL 2875-0024642 to -0024643)
- Attachment 6.2 Page 48 of Equipment Log (APL-MDL 2875-0024430 to -0024432)
- Attachment 6.3 Cleaning Procedure for Fluid bed processor FBP-250/500 (APL-MDL 2875-0024437 to -0024450)
- Attachment 6.4 Page # 81 Instruction Manual for Pam Glatt Fluid bed equipment FBE -250 (APL-MDL 2875-0024493 to -0024494)
- Attachment 6.5 Activity Qualification Report for measured surface roughness of inlet duct in Fluid Bed Processor (Document No. FU7-Unit VII-ACQR-0070 (APL-MDL 2875-0024816 to -0024825)
- Attachment 6.6 Meridan Review of Fluid Bed Processor Design and Operation to Confirm Conclusions Documented within PNC and 483 response (APL-MDL 2875-0024193 to -0024204)
- Attachment 6.7 Updated PMP checklist FU7-PMP-GEN-064 (APL-MDL 2875-0024283 to -0024287)

        - Attachment 7.1 Failure Investigation Report # APLUNIT07/ INV/ 045/ 19-00 (APL-MDL 2875-0024080 to -0024125)

- EIR Response (APL-MDL 2875-0009967)

- Organization Charts

    - APL Research Center-II (Organogram – ARD Lab – LCMS, NMR, PRP-HPLC & WS) (APL-MDL 2875-0031158)

    - Plant Organogram APL Unit-XI (APL-MDL 2875-0031157)

    - General Organogram of Formulation Division Unit-III (APL-MDL 2875-0031152)

    - Organogram of Formulation Division (Unit VII) – Main Block, Organogram of Quality Assurance Department – Main Block, Organogram of Quality Control Department – Main Block, Organogram of Manufacturing Department – Main Block, Compression Coating, Change Parts, Capsule Filling, Softgel, HVM, ARV (APL-MDL 2875-0031153 to -0031156)